Remarks

Claims 19-21 and 27-43 are pending. Claims 1-18 and 22-26 has been cancelled without prejudice. Applicants reserve the right to pursue the subject matter of any of the canceled claims in one or more divisional, continuation, or continuation-in-part applications.

Claim 21 has been rewritten in independent form. Claim 40 has been amended to correct an error in claim dependency. No new matter has been added.

Rejection Under §112

Claims 40-42 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite. The Examiner has pointed out an error in the recitation of claim dependency in claim 40. Applicants have corrected the error.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under §112.

Rejection Under §102

Claim 18 has been rejected under 35 U.S.C. §102(e) as being anticipated by International Publication WO 02/059321 (hereafter "De Francesco"). Applicants have canceled claim 18 solely in order to further prosecution.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under §102.

Rejection Under §103

Claims 18-20, 28-29, 31-34 and 37-38 have been rejected under 35 U.S.C. §103(a) as being anticipated by De Francesco in view of US Patent No. 6,297,003 (hereafter "Rice I") and International Publication WO 01/89364 (hereafter "Rice II") and further in view of US Patent No. 6,063,562 (hereafter "Melnick") and US Publication No. 2004/0018529 (hereafter "Li"). Applicants respectfully disagree.

De Francesco teaches HCV replicons with adaptive mutations to enhance replicon activity. The replicon sequences disclosed are that of HCV con-1, a consensus HCV sequence. De Francesco does disclose that other naturally occurring HCV 3' UTRs can be used. Although the 3' UTR from HCV-1a is not specifically mentioned, it is a naturally occurring UTR as the Examiner points out. However, broad, generic disclosures are inadequate to establish obviousness as to a species. *See Ashland Oil*, 776 F.2d at 296-97, 227 U.S.P.Q. at 666-67; *In re Jones*, 958 F.2d 347, 349-50, 21 U.S.P.Q. 2d 1941, 1943 (Fed. Cir. 1992) (disclosure of a genus in a prior art reference does not in itself render a species of that genus obvious).

The Examiner cites Rice I as disclosing a number of HCV-1a 3' UTR sequences. The Examiner contends that "those of ordinary skill in the art would have been motivated to make such substitutions because the art indicates that the 3' UTRs of Rice are functional equivalents for the sequences provided in De Francesco" (see page 6, lines 2-4 of the Office Action mailed July 9, 2007). However, the Examiner has provided none of the art that describes the 3' UTRs of HCV con-1 and HCV-1a as equivalent. The rejection of a claim based on the Examiner's opinion, without additional evidence, is impermissible. *In re Zeidler*, 682 F.2d 961, 967 (CCPA 1982). To the extent that the Examiner is relying on facts within his/her personal

knowledge, Applicants respectfully request an affidavit of the Examiner pursuant to 37 C.F.R. § 1.107(b).

The Examiner admits that neither De Francesco nor Rice I teach or suggest using HCV NS5B from clinical isolates in the disclosed replicons. The Examiner cites to De Francesco and Rice II as teaching that HCV replicons can contain sequences from different HCV subtypes or strains. The Examiner combines this teaching with the teaching from Rice II that replicons can be used to screen for anti-viral compounds and should have "wild type" sequences to allegedly suggest use of clinical isolate sequences. Applicants note that HCV sequences evolve during infection and incorporate adaptive mutations to better replicate in their particular cellular environment. As such, clinical isolate sequences are generally *not* "wild type". One skilled in the art would not interpret the teachings of Rice II as referring to clinical isolate sequences. Even assuming *en arguendo* that the reference to "wild type" in Rice II does mean a clinical isolate sequence, Applicants still fail to see how such a statement would be interpreted by one skilled in the art as pertaining to the cited statements concerning sequences from different HCV subtypes or strains to arrive at the claimed chimeric replicons.

The Examiner also cites Melnick and Li as teaching the use of clinical isolate sequences. Melnick is directed to methods of predicting the identity of HIV protease mutants that emerge in response to drug treatment. Applicants note that throughout Melnick, clinical isolate sequences are referred to as "mutant" rather than "wild type" as in Rice II. The passage cited by the Examiner as having relevance to the instant application (*i.e.*, column 11) is directed to the use of their disclosed methods to evaluate the efficacy of a drug against various proteases, some of which can be mutant forms from clinical isolates.

Li is directed to methods of cloning genes encoding proteins involved in proteolytic cleavages and methods of finding protease inhibitors. The passage cited by the Examiner as having relevance to the instant application (*i.e.*, paragraph 9) is in the Background section of Li where identification of protease inhibitors are said to be important because a number of viruses use proteases in their life cycle. Li proposes that their disclosed methods can be adapted to screen clinical isolates of HIV for drug resistance.

Applicants point out that neither Melnick nor Li are directed to HCV or the use of any methods using a replicon. The mere mention of using clinical isolates of other viruses for other purposes would not lead one skilled in the art to interpret the teachings of De Francesco, Rice I or Rice II in the way the Examiner alleges.

The test is not whether each difference individually is obvious; rather, it is whether the claimed invention as a whole is obvious. *In re Buehler* (CCPA 1975) 515 F2d 1134, 185 USPQ 781. Applicants contend that the Examiner has shown no reason why one skilled in the art would pick and choose the cited teachings and combine them.

Applicants submit that any rejection of the instant claims under § 103 would indicate the improper use of hindsight gained from Applicants' own specification. Hindsight should be avoided in applying the nonobviousness requirement. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed. Cir. 1987), *cert. denied*, 481 U.S. 1052 (1987). Without the benefit of hindsight, the teachings of the references cited by the Examiner, alone or in combination, could not render obvious the claimed invention. As such, a finding of obviousness could only be arrived through a prohibited procedure in which "the claims were used as a frame, and individual naked parts of separate prior art references were employed

as a mosaic to recreate a facsimile of the claimed invention." *W.L. Gore & Assocs. Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1552, 220 U.S.P.Q. 303, 312 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under §103.

Claims 35 and 36 have been rejected under 35 U.S.C. §103(a) as being anticipated by De Francesco in view of Rice I, Rice II, Melnick and Li in view of US Patent 5,783,669 (hereafter "Hawkins"). Applicants respectfully disagree.

As discussed *supra*, De Francesco, Rice I, Rice II, Melnick and Li do not render the claimed invention obvious. If the base claim from which a claim depends is not made obvious by the cited references, then the dependant claim is not obvious over those same references as well.

Hawkins is cited to show that modifications to nucleic acid sequences could be made without affecting the encoded amino acid sequence. Applicants contend that this does nothing to remedy the deficiencies of De Francesco, Rice I, Rice II, Melnick and Li.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under §103.

Double Patenting

Claims 18-20, 28, 29, 31-34, 37, and 38 have been provisionally rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims 9 and 10 of

co-pending application Serial No. 10/543,633 (hereafter "'633 application"). Applicants respectfully request that this rejection be withdrawn until such time that there is at least one issued claim in either the '633 application or the instant application.

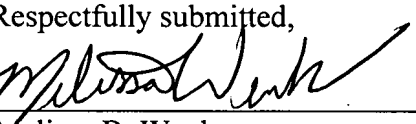
Conclusion

It is believed that the claims now pending are in condition for allowance. Early and favorable action by the Examiner is earnestly requested.

Authorization

The Commissioner is hereby authorized to charge to deposit account 13-2755 $120.00 to pay the fee under 37 C.F.R. §1.136(a) for an Extension of Time for one month. Additionally, the Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to deposit account 13-2755.

Respectfully submitted,

Dated: November 5, 2007 By: 

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